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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/087,871	06/02/1998	GERALD WAGNER	0708-4038	1082

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EXAMINER
GABEL, GAILENE

ART UNIT	PAPER NUMBER
1641	20

DATE MAILED: 04/07/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/087,871	WAGNER, GERALD	
	Examiner	Art Unit	
	Gailene R. Gabel	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 January 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-21* is/are pending in the application.

4a) Of the above claim(s) *13-21* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-12* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-21* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a)☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1)☒ Notice of References Cited (PTO-892)
2)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3)☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4)☐ Interview Summary (PTO-413) Paper No(s). _____ .
5)☐ Notice of Informal Patent Application (PTO-152)
6)☐ Other: .

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 1/10/03 has been entered.

Amendment Entry

2. Applicant's amendment and response filed 1/10/03 in Paper No. 19 is acknowledged and has been entered. Claims 1, 9, and 10 have been amended. Currently, claims 1-21 are pending. Claims 1-12 are under examination.

Rejections Withdrawn

Claim Rejections - 35 USC § 112

3. In light of Applicant's amendment, the rejection of claims 1-12 under 35 U.S.C. 103(a) as being unpatentable over Lillig et al. (US 4,965,049) in view of Groth et al. (US 5,690,103) and in further view of Furlong et al. (Clinical Chemistry, 1990), is hereby, withdrawn.

New Grounds of Rejection

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 1-12 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is vague and indefinite because it is unclear what Applicant intends to encompass in reciting, "wherein the hierarchical decision-tree organization includes at least a plurality of paths of the biochemical marker measurement steps". It is further unclear as recited what effectively determines these plurality of paths so as to require one measurement type in one instance and not another in instance. Please clarify.

Same analogous comments and problems apply to claims 9 and 10.

New Matter

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 1-12 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

In this case, the specification does not appear to provide literal or descriptive support for the recitation of "reflex algorithm ... represents a hierarchical decision-tree organization of biochemical marker measurement steps, each of the biochemical marker measurement steps specifying a measurement set comprising ..., wherein at least two of the biochemical marker measurement steps specify non-identical measurement sets, and wherein the hierarchical decision-tree organization includes at least a plurality of paths of the biochemical marker measurement steps wherein at least one of the plurality of paths of the biochemical marker measurement steps includes an immunoassay measurement type and/or a clinical chemistry measurement type not required by another of said plurality of paths of the biochemical marker measurement steps ". Applicant throughout the specification describes certain biochemical marker measurement steps to identify a pathology such as acute myocardial infarct (AMI) but fails to provide literal support for such recitation in claims 1, 9, and 10 defining reflex algorithm. Further, none of the originally filed claims recited the limitation in question. Recitation of claim limitation lacking literal support in the specification or originally filed claims constitutes new matter.

Scope of Enablement

6. Claims 1-12 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for reflex algorithm testing for AMI using cardiac biochemical markers to diagnose AMI, does not reasonably provide enablement for reflex algorithm testing of any other biochemical markers for diagnosis of any pathology

such as parasitic infection or viral infection or cancer. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

As set forth in *In view of the teachings of In re Wands, 8 USPQ2d 1400*, enablement requires that the specification teach those skilled in the art to make and use the invention without undue experimentation. Factors to be considered in determining, whether a disclosure would require undue experimentation include 1) the nature of the invention, 2) the state of the prior art, 3) the predictability or lack thereof in the art, 4) the amount of direction or guidance present, 5) the presence or absence of working examples, 6) the quantity of experimentation necessary, 7) the relative skill of those in the art, and 8) the breadth of the claims.

The nature of the invention- the invention is directed to a diagnostic system comprising an immunoassay analyzer, a clinical chemistry analyzer, an automatic sample handling device, and a processor used to perform biochemical marker measurement tests to facilitate diagnosis of AMI pathology according to a reflex algorithm.

The state of the prior art- the prior art of record fails to disclose a diagnostic system comprising an immunoassay analyzer, a clinical chemistry analyzer, an automatic sample handling device, and a processor used to perform biochemical marker measurement tests to facilitate diagnosis of any pathology including viral infection or cancer, according to a reflex algorithm.

The predictability or lack thereof in the art- there is no predictability based on the instant specification that the claimed diagnostic system will work for performing biochemical marker measurement tests to facilitate diagnosis of any pathology known to man, according to a reflex algorithm.

The amount of direction or guidance present- appropriate guidance is provided by the specification for the claimed diagnostic system to work in facilitating diagnosis of AMI according to a reflex algorithm. However, no guidance is provided by the specification for the claimed system to work in facilitating diagnosis of any pathology known to man according to reflex algorithm.

The presence or absence of working examples- working examples are provided in the specification that uses the diagnostic system to perform biochemical marker measurement tests to facilitate diagnosis of AMI according to a reflex algorithm. There are no working examples that show analogous results in performing biochemical marker measurement tests to facilitate diagnosis of any pathology known to man according to a reflex algorithm, which are encompassed by the broad scope of the instant claims.

The quantity of experimentation necessary- it would require undue amount of experimentation for the skilled artisan to make and use the diagnostic system as claimed.

The relative skill of those in the art-the level of skill in the art is high.

The breadth of the claims- as recited, the instant claims are directed to a diagnostic system comprising an immunoassay analyzer, a clinical chemistry analyzer, an automatic sample handling device, and a processor used to perform biochemical

marker measurement tests to facilitate diagnosis of a pathology according to a reflex algorithm. As recited, the instant diagnostic system can facilitate diagnosis of a pathological condition according to a reflex algorithm, regardless of the type of pathology, i.e. infection or cancer, present in a patient.

While AMI diagnostic systems and methods which establish use of biochemical marker tests in a reflex algorithm for patients with suspected MI are illustrated and described in the specification, there is no showing of any working examples of the claimed system for use in the diagnosis of any other pathological condition. The fact that the claimed diagnostic system appears to work for biochemical markers of AMI in patients suspected of MI is not sufficient to enable the breadth of the claimed system for diagnosing any and all pathologies known to man, i.e. cancer or bacterial infection. The specification does not establish a direct correlation between MI and other pathologies which would lead the skilled artisan to say that if the claimed system and method works for providing quick diagnosis of MI, then it should work in all pathological conditions to enable the breadth of the claimed method. While it is not necessary to show working examples for every possible embodiment, there should be sufficient teachings in the specification that would suggest to the skilled artisan that the breadth of the claimed method is enabled. This is not the case in the instant specification. Thus, the claimed system is only enabled for diagnosing AMI using the claimed reflex algorithm.

In view of the teachings of *In re Wands, 8 USPQ2d 1400*, it has been determined that the level of experimentation required to enable the breadth of the claims is undue. It has been set forth above that 1) the experimentation required to enable the claimed

system and method for diagnosing any and all pathological conditions known to man, would be great, as 2) there is no experimental evidence provided that would indicate that the claimed system would work in diagnosing pathologies, other than AMI in patients suspected of having AMI; 3) there is no proper guidance that shows that biochemical markers known to diagnose AMI in a reflex algorithm can be correlated for application with any and all pathologies in the instant specification, 4) the nature of the invention is a diagnostic system that would perform biochemical marker measurement tests to facilitate diagnosis of AMI pathology according to a reflex algorithm, 5) the relative skill of those in the art is high, yet 6) the state of the prior art has been shown to be unpredictable as evidenced by the fact that no prior art has been cited that shows a diagnostic system that would perform biochemical marker measurement tests to facilitate diagnosis of any and all pathological conditions according to a reflex algorithm, and lastly 7) the claims broadly recite a diagnostic system for performing biochemical marker measurement tests to facilitate diagnosis of a pathology according to a reflex algorithm, regardless of the type of pathology, i.e. infection or cancer, present in a patient, without specifically stating how this can be done without undue experimentation.

Therefore, it is maintained that one of ordinary skill in the art could not make and use the invention as claimed without undue experimentation.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. Claims 1-12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lillig et al. (US 4,965,049) in view of Cantantore et al. (US 5,772,963) and in further view of Aziz et al. (Journal of Cellular Biochemistry, Supp. 17G, pp. 247 (1993)).

Lillig discloses a clinical chemistry analyzer system combining analyzers, each adapted for independent operation and each possessing different operational characteristics for different applications wherein each modular analyzer is adapted to operate as a portion of a system of modular analyzers (see column 2, lines and 8-26 and Figure 3). The system includes a first analyzer and a second analyzer each including a sample carousel, analyzing means, and automated probe means for transferring samples from the sampling carousels to the analyzing means. A processor is in communication with the analyzers wherein electronic and electrical interfaces form public and/or private networks between the analyzers so as to form the system. Operational information and instructions are coded into the analyzers through a disk drive (see column 6, lines 51-65).

Lillig differs from the instant invention in failing to disclose that one of the analyzers is specifically an immunoassay analyzer. Lillig further differs from the instant invention in failing to disclose incorporating a hematology analyzer into the diagnostic system comprising clinical chemistry analyzer and immunoassay analyzer.

Cantantore et al. disclose an analytical system for performing analyses on test samples in instruments for performing a series of tests using different reagents and aliquots. The analytical system is comprised of subcomponents and modules which are applicable to broad range analyzer types including immunoassay analyzers, chemistry analyzers, flow cytometers, and hematology analyzers. The analytical system utilizes a Control Area Network (CAN) and nodal architecture in the instrument with functions and logic distributed throughout the Nodes. A main processor (system controller) is connected on one hand to an operator input device for controlling the system, and on the other hand to microprocessors (microcontrollers) for performing autonomously a variety of functions of the system. The CANBUS permits distributed logic to be implemented throughout the system (see columns 1-3 and 56).

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to incorporate the analytical system disclosed by Cantantore including an immunoassay analyzer and a hematology analyzer in cooperation with the system, into the analyzer system disclosed by Lillig because Lillig specifically taught combining with the clinical chemistry analyzer, other analyzers, each adapted for independent operation and possessing different operational characteristics for different applications and Cantantore specifically taught that subcomponents and modules can be combined for use in an analytical system involving clinical chemistry analyzers, immunoassay analyzers, and hematology analyzers.

Lillig and Cantantore differ from the instant invention in failing to disclose that the processor commands the clinical chemistry analyzer and immunoassay analyzer to

execute measurements specified by a program to facilitate diagnosis of a pathology according to a reflex algorithm.

Aziz et al. teach reflexive algorithmic approach to clinical decision-making using breast cancer as a model. Aziz et al. specifically taught applying a Bayesian probability approach to data in order to derive a branched tree algorithm to predict survival rates for both lymph node-positive and lymph node-negative women with breast cancer. The size of the algorithm was reduced to ensure the most information while minimizing the number of tests requested; thus, reducing cost.

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to incorporate the teaching of Aziz in reflexive algorithmic approach to diagnosis of a disease into the diagnostic analytical system disclosed by Lillig as modified by Cantantore because Lillig and Cantantore specifically taught advantage of simultaneous and fast speed analysis of relevant biochemical tests in diagnosing specific life-threatening conditions and Aziz specifically taught that reflexive algorithmic approach further provides advantage in fast speed analysis by minimizing the amount of biochemical tests performed by analyzers while obtaining the most information and reducing cost using the probability approach to derive branch tree algorithm.

Response to Arguments

8. Applicant's arguments with respect to claims 1-12 have been considered but are moot in view of the new grounds of rejection.

9. No claims are allowed.

Remarks

10. Prior art made of record are not relied upon but considered pertinent to the applicants' disclosure:

Groth et al. (US 5,690,103) teaches computer based neural networks design incorporated into analyzers where measured patient results (analyte concentrations, enzymatic activities, etc.) are compared and referenced with biochemical marker standards from preclassified example cases to provide an indication of a pathology. Groth discloses that the computer system is designed to perform specific computational tasks to support a decision tree that provides a feedback mechanism of what subsequent measurements are to be performed based on the most recent measure; the end product of which provides a diagnostic indication of a pathology (see column 5 and column 8).

Furlong et al. (Clinical Chemistry, 1990) teaches computerized neural network analysis specifically of cardiac data for use as clinical decision-making aid wherein computer hardware and software emulate biological nervous systems formed by interconnected artificial neurons (see page 135, column 1, first full paragraph). Such artificial intelligence programs use algorithmic process for decision making wherein clinicians knowledge has been distilled in a hierarchy of facts or rules wherein the matrix of synaptic weighting factors are calculated using back propagation, supervised learning algorithm (see page 134, column 2, last paragraph).

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gail Gabel whose telephone number is (703) 305-0807. The examiner can normally be reached on Monday to Thursday from 7:00 AM to 4:30 PM. The examiner can also be reached on alternate Fridays from 7:00 AM to 3:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on (703) 308-3399. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Christopher L. Chin

CHRISTOPHER L. CHIN
PRIMARY EXAMINER
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4/4/03

Gailene R. Gabel
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